## PACKAGE INSERT

**SCHEDULING STATUS:** S4

**PROPRIETARY NAME AND DOSAGE FORM:**

**Pharma-Q Bupivacaine Injection 50 mg/10 ml** solution

**COMPOSITION:**

Each 10 ml contains:

Bupivacaine hydrochloride monohydrate equivalent to bupivacaine hydrochloride anhydrous 50 mg.

Excipients: sodium hydroxide and water for injections.

**PHARMACOLOGICAL CLASSIFICATION:**

A 4 Local anaesthetics

**PHARMACOLOGICAL ACTION:**

**Pharmacodynamic properties:**

Bupivacaine hydrochloride is a local anaesthetic of the amide type. It is a potent agent capable of producing prolonged anaesthesia due to its amide structure. Bupivacaine hydrochloride stabilizes the neuronal membrane and prevents initiation and transmission of nerve impulses, thereby acting as a local anaesthetic. When administered in recommended doses and concentrations, it does not ordinarily produce irritation or tissue damage and does not cause methaemoglobinaemia.



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**Pharmacokinetic properties:**

**Absorption:**

The onset of action of bupivacaine hydrochloride is rapid and anaesthesia may last for several hours. The duration of action (up to 8 hours) is significantly longer than any other commonly used local anaesthetic.

**Distribution:**

Bupivacaine hydrochloride is about 95 % bound to plasma protein. It has a half- life of 1,5 to 5,5 hours in adults and 8 hours in neonates.

**Metabolism:**

Due to the amide structure, bupivacaine hydrochloride is not detoxified by plasma esterases. It is metabolized in the liver.

**Elimination:**

Bupivacaine hydrochloride is excreted in the urine principally as metabolites with only 5 % to 6 % as unchanged medicine. Bupivacaine is excreted into breast milk in small quantities and crosses the placenta but the ratio of foetal concentration to maternal concentrations is relatively low. Bupivacaine also diffuses into the cerebrospinal fluid.

**INDICATIONS:**

**Pharma-Q Bupivacaine Injection 50 mg/10 ml** is indicated in:

Infiltration and regional nerve block including conduction anaesthesia when a prolonged effect is required.

**Pharma-Q Bupivacaine Injection 50 mg/10 ml** is therefore indicated in:

- peripheral nerve block
- caudal or epidural block.

**CONTRAINDICATIONS:**

**Pharma-Q Bupivacaine Injection 50 mg/10 ml** is contraindicated for use in:

- patients with a known hypersensitivity to bupivacaine hydrochloride or to any other local anaesthetic agents of the amide-type
- patients with low plasma cholinesterase concentrations or those receiving anti-cholinesterases
- patients who are under twelve years of age (see **DOSAGE AND DIRECTIONS FOR USE**)
- patients who require **intravenous** regional anaesthesia
- patients who require **paracervical** block in obstetrics (see **PREGNANCY AND LACTATION**).
- patients with cerebrospinal diseases or altered coagulant status (Techniques such as epidural anaesthesia should not be employed in these patients)
- patients who are pregnant (other than in labour) or lactating as the safety in pregnancy and lactation has not been established. Bupivacaine hydrochloride may be excreted into breast milk in small quantities (see **PREGNANCY AND LACTATION**).

**WARNINGS and SPECIAL PRECAUTIONS:**

**ALWAYS HAVE RESUSCITATION EQUIPMENT AND MEDICATION AT HAND WHEN ANY LOCAL ANAESTHETIC IS USED (see DOSAGE AND DIRECTIONS FOR USE)**

**Pharma-Q Bupivacaine Injection 50 mg/10 ml:**

- appears to be more cardiotoxic than other local anaesthetics
- fatalities have occurred since toxicity is difficult to treat
- the central nervous system and cardiac toxicity can be enhanced by hypoxia and acidosis.



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**Special Precautions with local aneasthetics:**

- hypotension often accompanies spinal and epidural anaesthesia
- inappropriate positioning of the patient may be a contributory factor for women in labour
- foetal intoxication may occur following the use of local anaesthetics in labour
- local anaesthetics should be given with caution to the elderly, debilitated patients (see **DOSAGE AND DIRECTIONS FOR USE**) as well to patients with epilepsy, impaired cardiac conduction or impaired and/or hepatic damage
- patients with myasthenia gravis may be particularly susceptible to the effects of local anaesthetics.

**Effects on the ability to drive and use machines:**

Patients should be instructed that they should avoid potentially hazardous tasks such as driving and operating machinery until they know how **Pharma-Q Bupivacaine Injection 50 mg/10 ml** affects them.

**INTERACTIONS:**

None known.

**PREGNANCY AND LACTATION:**

For **Pharma-Q Bupivacaine Injection 50 mg/10 ml:**

- safety in pregnancy and lactation (other than in labour) has not been established (see **CONTRAINDICATIONS**)
- the use of local anaesthetics during pregnancy in the presence of foetal hypoxia or acidosis may be dangerous

- foetal bradycardia frequently follows paracervical block with some amide-type local anaesthetics and may be associated with foetal acidosis (see **CONTRAINDICATIONS**)
- added risk appears to be present in prematurity, toxaemia of pregnancy and foetal distress.

**DOSAGE AND DIRECTIONS FOR USE:**

**Pharma-Q Bupivacaine Injection 50 mg/10 ml:**

- Dosage varies and depends upon:
    - the site to be anaesthetized
    - the area thereof.
    - the vascularity of the tissues.
    - the number of neuronal segments to be blocked.
    - individual tolerance.
    - the technique employed.
- in recommended doses, it produces complete sensory block, but the effect on motor function differs depending on volume utilized
- the duration of anaesthesia is such that for most indications, a single dose is sufficient
- is not recommended for children younger than 12 years (see **CONTRAINDICATIONS**)
- the total dose administered over a period of 4 hours should not be exceeded unless there are special considerations present
- the maximum recommended dose in a single injection is 150 mg
- where a dosage is calculated on a patients mass, this should not exceed 2 mg per kg body mass, i.e. 20 to 30 ml of the 0,5 % m/v injection or 150 mg for adults
- doses should be reduced and given with caution to the elderly or debilitated Patients (see **WARNINGS and SPECIAL PRECAUTIONS**)

- any unused portion should be discarded. If the solution contains a precipitate or is discoloured, it should not be used.

**General Dosages:**

- **Regional nerve block:** 5 to 30 ml (25 to 150 mg).
- **Surgical procedures-lumbar epidural block:** 10 to 20 ml (50 to 100 mg).

The dosages given in the table below are more specific and can be used as a general guide for use in the average adult:

| **Procedure:** | **Dose:** | | **Remarks:** |
|---|---|---|---|
| | **ml** | **mg** | |
| **Trigeminal block** | 0,5 - 4 | 2,5 - 20 | |
| **Axillary block** | 15 - 30 | 75 - 150 | |
| **Intercostal block** | 3 - 5 | 15 - 25 | The dose indicated is for every segment. |
| **Epidural anaesthesia** | 10 - 20 | 50 - 100 | |
| **Continuous epidural anaesthesia** | | Initially 10 ml followed by 3-5-8 ml every 4 - 6 hours. The dose depends on the number of segments to be rendered analgesic and the patient's age. | |
| **Caudal anaesthesia** | 15 – 30 | 75 – 150 | |



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**SIDE EFFECTS:**

**Pharma-Q Bupivacaine Injection 50 mg/10 ml** may have side effects**:**

- side effects apparent after local anaesthesia may be due to the anaesthetic or to errors in technique or may be the result of blockade of the sympathetic nervous system
- local anaesthetics may have systemic adverse effects as a result of the raised plasma concentrations, which ensue when the rate of absorption into the circulation exceeds the rate of breakdown
- the systemic toxicity of local anaesthetics mainly involves the central nervous system and the cardiovascular system

The following side effects may occur and the frequencies are unknown:

**Immune system disorders:**

*Frequency unknown:*

Hypersensitivity reactions which are characterized by cutaneous lesions (e.g. urticaria), oedema and other manifestations of allergy.

**Nervous system disorders:**

*Frequency unknown:*

Excitation or depression. Excitation of the central nervous system may be manifested by restlessness, excitement, nervousness, dizziness, tinnitus, blurred vision, nausea and vomiting, muscle twitching, tremors, and convulsions.

Numbness of the tongue and perioral region may appear as an early sign of systemic toxicity. Excitation may be transient and followed by depression of the nervous system with drowsiness, respiratory failure and coma.

**Cardiovascular disorders:**

*Frequency unknown:*

There may be effects on the cardiovascular system with myocardial depression and peripheral vasodilation resulting in hypotension and bradycardia; arrhythmias and cardiac arrest may occur.

**KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:**

See **SIDE EFFECTS** and **WARNINGS and SPECIAL PRECAUTIONS**.

Over dosage should be treated symptomatically and supportive measures should be taken

- When systemic reactions to local anaesthetics occur, steps should be taken to maintain the circulation, respiration and to control convulsions
- Therefore, resuscitation equipment and medication should always be at hand for emergencies (see **Boxed warning** in the **WARNINGS and SPECIAL PRECAUTIONS** section)
- The physician should maintain the patient's airway and support ventilation with oxygen.
- Convulsions may be controlled with oxygen and intravenous administration of diazepam, thiopentone sodium, or short-acting barbiturates.
- It should be remembered that anti-convulsant treatment may also depress respiration and the circulation.
- A short acting neuromuscular blocking agent, together with endotracheal intubation and artificial respiration, may be used when convulsions persist.
- The circulation should be maintained with the infusion of plasma or intravenous fluids.
- Vasopressor agents, where appropriate, may be used in the treatment of marked hypotension although their use is accompanied by a risk of central nervous system

excitation.

- Vasopressor should not be given to patients receiving oxytocic [~~drugs~~] medicines.

**IDENTIFICATION:**

A clear, colourless or almost colourless solution in 10 ml clear colourless glass ampoules.

**PRESENTATION:**

A clear colourless glass ampoule containing a 0,5 % m/v solution of bupivacaine hydrochloride in 10 ml ampoules. 10 Ampoules per box.

**STORAGE INSTRUCTIONS:**

Store at or below 25 °C.

Keep out of reach of children.

Protect from light.

**REGISTRATION NUMBER:**

31/4/0007

**NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:**

PHARMA-Q HOLDINGS (PTY) LTD

50 COMMANDO ROAD

INDUSTRIA WEST 2003

JOHANNESBURG



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SOUTH AFRICA

**DATE OF PUBLICATION OF THE PACKAGE INSERT:**

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